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<110> Larsen, Bjarne Due
<120> PHARMACOLOGICALLY ACTIVE PEPTIDE CONJUGATES HAVING A
      REDUCED TENDENCY TOWARDS ENZYMATIC HYDROLYSIS
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<150> DK 0317/98
<151> 1998-03-09
<160> 121
<170> PatentIn Ver. 2.0
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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<223> exendin-3
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Ser Gly Ala Pro Pro Pro Ser
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Glu Tyr Leu
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Asp Leu Arg Val Asp Thr Lys Ser Arg Ala Ala Trp Ala Arg Leu Leu
Gln Glu His Pro Asn Ala Arg Lys Tyr Lys Gly Ala Asn Lys Lys Gly
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Leu Ser Lys Gly Cys Phe Gly Leu Lys Leu Asp Arg Ile Gly Ser Met
Ser Gly Leu Gly Cys
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 Ser Asp Ala Ala Val Asp Thr Ser Ser Glu Ile Thr Thr Lys Asp Leu
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Cys Phe Ile Gln Asn Cys Pro Xaa Gly
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Xaa Cys Phe Xaa Lys Thr Cys Xaa
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Ala Cys Asp Thr Ala Thr Cys Val Thr His Arg Leu Ala Gly Leu Leu
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Ser Arg Ser Gly Gly Val Val Lys Asn Asn Phe Val Pro Thr Asn Val
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Gly Ser Lys Ala Phe
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Tyr Pro Phe Phe
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Phe Gly Gly Phe Thr Gly Ala Arg Lys Ser Ala Arg Lys Leu Ala Asn
Gln
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Asp Arg Val Tyr Ile His Pro Phe His Leu Val Ile His
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<211> 12
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<213> Homo sapiens
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<223> Hyp
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Gly Pro Xaa Gly Ala Gly
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Ile Leu Pro Trp Lys Trp Pro Trp Pro Trp Arg Arg
<210> 44
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<223> osteocalcin (37-49)
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Gly Phe Gln Glu Ala Tyr Arg Arg Phe Tyr Gly Pro Val
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Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys
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<210> 49
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<213> Artificial Sequence
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His His Leu Gly Gly Ala Lys Gln Ala Gly Asp Val
<210> 50
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Asn Val Ile Gln Ile Ser Asn Asp Leu Glu Asn Leu Arg
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 <223> D-Pro
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Tyr Pro Trp Gly
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Thr Arg Ser Ala Trp
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 Asp Arg Val Tyr Ile His Pro Phe His Leu Val Ile His Asn
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 Lys Lys Lys
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<223> Xaa at various positions throughout the sequence
     may be Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp,
     Glu, Arg, His, Met, Orn, Dbu or Dpr
<400> 82
Lys Lys Xaa Lys Xaa
<210> 83
<211> 6
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Stabilising peptide
<220>
<223> Xaa at various positions throughout the sequence
      may be Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp,
      Glu, Arg, His, Met, Orn, Dbu or Dpr
<400> 83
Lys Lys Lys Xaa Xaa
<210> 84
<211> 6
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Stabilising peptide
<400> 84
Lys Glu Lys Glu Lys Glu
<210> 85
<211> 6
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Stabilising peptide
<400> 85
Glu Lys Glu Lys
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<210> 86
<211> 6
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Stabilising peptide
<400> 86
Lys Lys Glu Glu Glu
<210> 87
<211> 6
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Stabilising peptide
<400> 87
Glu Glu Glu Lys Lys
<210> 88
<211> 50
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: GHRH (1-44)-Lys6
<400> 88
Tyr Ala Asp Ala Ile Phe Thr Asn Ser Tyr Arg Lys Val Leu Gly Gln
Leu Ser Ala Arg Lys Leu Leu Gln Asp Ile Met Ser Arg Gln Gln Gly
Glu Ser Asn Gln Glu Arg Gly Ala Arg Ala Arg Leu Lys Lys Lys
Lys Lys
      50
<210> 89
 <211> 50
 <212> PRT
 <213> Artificial Sequence
 <223> Description of Artificial Sequence: GHRH (1-44)-Glu6
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<400> 89 Tyr Ala Asp Ala Ile Phe Thr Asn Ser Tyr Arg Lys Val Leu Gly Gln Leu Ser Ala Arg Lys Leu Leu Gln Asp Ile Met Ser Arg Gln Gln Gly Glu Ser Asn Gln Glu Arg Gly Ala Arg Ala Arg Leu Glu Glu Glu Glu Glu 50 <210> 90 <211> 40 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: Lys6-PTH (1-34) <400> 90 Lys Lys Lys Lys Lys Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn Ser Met Glu Arg Val Glu Trp Leu Arg Lys 25 20 Lys Leu Gln Asp Val His Asn Phe <210> 91 <211> 40 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: PTH (1-34)-Lys6 <400> 91 Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn Ser Met Glu Arg Val Glu Trp Leu Arg Lys Leu Gln Asp Val His Asn Phe Lys Lys Lys Lys Lys 35 <210> 92 <211> 36 <212> PRT

<220>

<213> Artificial Sequence

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<223> Description of Artificial Sequence: GLP-1 (7-36)-Lys6
<400> 92
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
                                                          15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Lys Lys
Lys Lys Lys
         35
<210> 93
<211> 26
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: EMP-1-Lys6
<220>
<221> MOD RES
<222> (6)
<223> Cys(Acm)
<220>
<221> MOD_RES
<222> (15)
<223> Cys(Acm)
<400> 93
Gly Gly Thr Tyr Ser Xaa His Phe Gly Pro Leu Thr Trp Val Xaa Lys
Pro Gln Gly Gly Lys Lys Lys Lys Lys
<210> 94
<211> 26
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Lys6-EMP-1
<220>
<221> MOD_RES
 <222> (12)
<223> Cys(Acm)
 <220>
 <221> MOD_RES
 <222> (21)
 <223> Cys(Acm)
 <400> 94
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Lys Lys Lys Lys Lys Gly Gly Thr Tyr Ser Xaa His Phe Gly Pro
Leu Thr Trp Val Xaa Lys Pro Gln Gly Gly
<210> 95
<211> 32
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Lys6-EMP-1-Lys6
<220>
<221> MOD RES
<222> (12)
<223> Cys(Acm)
<220>
<221> MOD RES
<222> (21)
<223> Cys(Acm)
<400> 95
Lys Lys Lys Lys Lys Gly Gly Thr Tyr Ser Xaa His Phe Gly Pro
Leu Thr Trp Val Xaa Lys Pro Gln Gly Gly Lys Lys Lys Lys Lys
<210> 96
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: GHRP-(Lys)6
<220>
<221> MOD_RES
<222> (1)
<223> Aib
<220>
<221> MOD_RES
<222> (3)
<223> 2-D-Nal
<220>
<221> MOD RES
<222> (4)
<223> D-Phe
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<400> 96
Xaa His Xaa Xaa Lys Lys Lys Lys Lys Lys
                  5
<210> 97
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:
      Leu-enkephalin-Lys-Lys-Glu-Glu-Glu-Lys
<400> 97
Tyr Gly Gly Phe Leu Lys Lys Glu Glu Glu Lys
                  5
<210> 98
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:
      Leu-enkephalin-Lys-Glu-Glu-Glu-Lys
<400> 98
Tyr Gly Gly Phe Leu Lys Glu Glu Glu Lys
<210> 99
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Leu-enkephalin (Lys-Glu)3
<400> 99
 Tyr Gly Gly Phe Leu Lys Glu Lys Glu Lys Glu
                   5
 <210> 100
 <211> 11
 <212> PRT
 <213> Artificial Sequence
 <223> Description of Artificial Sequence: Leu-enkephalin-(Dpr)6
 <220>
 <221> MOD RES
 <222> (6)..(11)
 <223> Dpr
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<400> 100
Tyr Gly Gly Phe Leu Xaa Xaa Xaa Xaa Xaa
                  5
<210> 101
<211> 11
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Lys6-Leu-enkephalin
<400> 101
Lys Lys Lys Lys Lys Tyr Gly Gly Phe Leu
<210> 102
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:
      Lys6-Leu-enkephalin-Lys6
<400> 102
Lys Lys Lys Lys Lys Tyr Gly Gly Phe Leu Lys Lys Lys Lys
                                     10
Lys
<210> 103
<211> 16
<212> PRT
<213> Homo sapiens
<220>
<223> GnRH-Lys6
<400> 103
Glu His Trp Ser Tyr Gly Leu Arg Pro Gly Lys Lys Lys Lys Lys Lys
<210> 104
<211> 16
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: GnRH-(Lys-Glu)3
<400> 104
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Glu His Trp Ser Tyr Gly Leu Arg Pro Gly Lys Glu Lys Glu
<210> 105
<211> 40
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: PTH 1-34 (Lys-Glu)3
<400> 105
Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn
                  5
Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His
             20
                                 25
Asn Phe Lys Glu Lys Glu Lys Glu
                            40 .
         35
<210> 106
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Leu-enkephalin-(Orn)6
<220>
<221> MOD_RES
<222> (6)..(11)
<223> Orn
<400> 106
Tyr Gly Gly Phe Leu Xaa Xaa Xaa Xaa Xaa
<210> 107
<211> 11
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Leu-enkephalin-(Dbu)6
<220>
<221> MOD RES
 <222> (6)..(11)
 <223> Dbu
 <400> 107
 Tyr Gly Gly Phe Leu Xaa Xaa Xaa Xaa Xaa
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<210> 108
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Leu-enkephalin-(Dpr)6
<221> MOD RES
<222> (6)..(11)
<223> Dpr
<400> 108
Tyr Gly Gly Phe Leu Xaa Xaa Xaa Xaa Xaa Xaa
                  5
<210> 109
<211> 15
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Leu-enkephalin-Lys10
<400> 109
Tyr Gly Gly Phe Leu Lys Lys Lys Lys Lys Lys Lys Lys Lys
                  5
<210> 110
<211> 9
<212> PRT
<213> Homo sapiens
<220>
<223> DSIP
<400> 110
Trp Ala Gly Gly Asp Ala Ser Gly Glu
<210> 111
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Substance P-Lys6
<400> 111
Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu Met Lys Lys Lys Lys
                                                         15
Lys
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<210> 112
<211> 11
<212> PRT
<213> Homo sapiens
<220>
<223> Substance P
<400> 112
Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu Met
                  5
<210> 113
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Lys6-Substance P
<400> 113
Lys Lys Lys Lys Lys Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu
Met
<210> 114
<211> 11
<212> PRT
<213> Artificial Sequence
 <223> Description of Artificial Sequence: Lys6-GHRP
 <220>
 <221> MOD RES
 <222> (7)
 <223> Aib
 <220> .
 <221> MOD_RES
 <222> (9)
 <223> 2-D-Nal
 <220>
 <221> MOD_RES
 <222> (10)
 <223> D-Phe
 <400> 114
 Lys Lys Lys Lys Lys Xaa His Xaa Xaa Lys
   1
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<210> 115
<211> 10
<212> PRT
<213> Homo sapiens
<220>
<223> GnRH
<220>
<221> MOD RES
<222> (1)
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<400> 115
Xaa His Trp Ser Tyr Gly Leu Arg Pro Gly
 1 5
<210> 116
<211> 16
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Lys6-GnRH
<400> 116
Lys Lys Lys Lys Lys Gln His Trp Ser Tyr Gly Leu Arg Pro Gly
<210> 117
<211> 20
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: EMP-1
<400> 117
Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
Pro Gln Gly Gly
             20
<210> 118
<211> 30
<212> PRT
<213> Homo sapiens
<220>
<223> GLP-1-(7-36)
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<400> 121

Tyr Gly Gly Phe Leu Glu Glu Lys Glu Glu Glu

<400> 118 His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg 20 25 <210> 119 <211> 34 <212> PRT <213> Homo sapiens <220> <223> PTH (1-34) <400> 119 Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn 5 Ser Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His 30 25 Asn Phe <210> 120 <211> 11 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: Leu-enkephalin-Lys-(Glu)3-(Lys)2 Tyr Gly Gly Phe Leu Lys Glu Glu Glu Lys Lys <210> 121. <211> 11 <212> PRT <213> Homo sapiens <223> Leu-enkephalin-(Glu2-Lys-Glu3)